TOTAL MASS CONTROL IN UNCERTAIN COMPARTMENTAL SYSTEMS

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Abstract: In this paper we analyse the control of the total mass of compartmental systems, under the presence of uncertainties. We consider a control law that has a very good performance when applied to compartmental systems without uncertainties and show that, even when the system parameters are not exactly known, that good performance is maintained. In fact, for a wide class of compartmental systems of R^3, it is possible to prove that, when we apply that control law to the real system, the total mass of the system converges to a positive constant value, which depends on the parameter uncertainties and that can be made arbitrarily close to the desired mass, provided that the uncertainties in the parameter values are sufficiently small. The obtained results are illustrated by simulations for the control of the administration of the neuromuscular relaxant drug *atracurium* to patients undergoing surgery.

Keywords: Compartmental systems, positive control, uncertain systems, neuromuscular blockade control, full outflow connectedness.

1. INTRODUCTION

Compartmental models have been successfully used to model biomedical and pharmacokinetical systems, see, for instance, (Godfrey, 1983) or (Jacquez, 1993). This kind of systems consist of a finite number of subsystems, the compartments, which exchange matter with each other and with the environment. Such systems are positive systems (i.e., systems for which the state and output variables remain nonnegative whenever the input is nonnegative) and, as is well-known, in this case, the design of suitable control laws is more delicate, since one has to guarantee the positivity of the control input. In this framework, a nonnegative adaptive control law is proposed in (Haddad, 2003), in order to guarantee the partial asymptotic set-point stability of the closed loop system and a positive feedback control law is proposed in (Bastin, 2002), in order to stabilise the total system mass at an arbitrary set-point. In (Magalhaes, 2005) the same positive control law proposed in (Bastin, 2002) was used for the control of the neuromuscular blockade (see (Lemos, 1991), (Linkens, 1994) and (Mendonca, 1998)) of patients undergoing surgery, but no analysis was made of the effect of parameter uncertainty in its performance.

In this paper, we consider the control law proposed in (Bastin, 2002) and used in (Magalhaes, 2005), and analyse its performance for the control of the total mass of a wide class of compartmental systems, when the system parameters are not exactly known. Thus, we consider that the control law is tuned for a nominal process model that contains an additive uncertainty with respect to the real model, and analyse the behavior of the total mass in the controlled system. It turns out that, in this case, bounds for the asymptotical mass offset can be easily expressed in terms of the system uncertainties. Moreover, the total system mass converges to a positive constant value that depends on the value of the desired mass and on the uncertainties of the system parameters.

[1] This work was partially supported by FCT through the Unidade de Investigacao Matematica e Aplicacoes (UIMA), Universidade de Aveiro, Portugal.

2. COMPARTMENTAL SYSTEMS

Compartmental systems are dynamical systems described by a set of equations of the form

$$\dot{x_i} = \sum_{j \neq i} f_{ji}(x) - \sum_{l \neq i} f_{il}(x) - f_{i0}(x) + f_{0i}(x)$$
$$i = 1, \dots, n$$

(see (Godfrey, 1983) or (Sandberg, 1978)) where $x = (x_1, \dots, x_n)^T$ is the state variable and x_i and f_{ij} take nonnegative values. Each equation describes the evolution of the quantity or concentration of material within a subsystem, called compartment. Since the compartments exchange with each other and with the environment, in the above equation, x_i is the amount (or concentration) of material in compartment i, f_{ij} is the flow rate from compartment j to compartment i and the subscript 0 denotes the environment (see (Godfrey, 1983)). In this paper, we consider the class of linear time-invariant compartmental systems described by

$$\dot{x_i} = \sum_{j \neq i} k_{ji} x_j - \sum_{l \neq i} k_{il} x_i - q_i x_i + b_i u, \quad (1)$$

$i = 1, \dots, n$, where x_i and the input u take nonnegative values, $k_{ij}, q_i, b_i \in R_+$ and at least one b_i is positive (see Fig. 1).

Note that, in this case, $f_{ji} = k_{ji} x_j, f_{0i} = b_i u$ and $f_{i0} = q_i x_i$, and it can be easily proved that the system is positive, this is, if we consider an input u that remains nonnegative, then the state variable also remains nonnegative. Moreover, (1) can also be written in matrix form as

$$\dot{x} = Ax + bu, \quad (2)$$

where A (called compartmental matrix) is so that

$$a_{ii} = -q_i - \sum_{j \neq i} k_{ij} \text{ and, if } i \neq j, a_{ij} = k_{ji},$$

and $b = (b_1, b_2, \dots, b_n)^T$.

2.1 *Stabilisation*

The total mass of the system in a given state x is defined as $M(x) = \sum_{i=1}^{n} x_i$. For an arbitrary positive value M^*, the set $\Omega_{M^*} = \left\{x \in R_+^n : M(x) = M^*\right\}$ of all the points x in the state space with mass M^* is called an *iso-mass*.

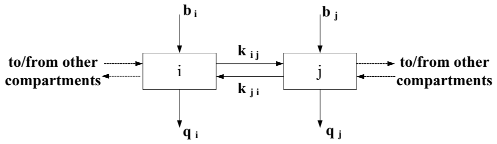


Fig. 1. Two compartments of a linear time-invariant compartmental model, as described by (1).

An important issue in the context of the control of compartmental systems that is to design a control law which yields a positive input that steers the system mass $M(x)$ to a desired value.

In (**?**), the following positive control law is proposed in order to guide the system trajectories to a given iso-mass Ω_{M*}:

$$\begin{aligned} u(x) &= \max\left(0, \tilde{u}(x)\right) \\ \tilde{u}(x) &= \left(\sum_{i=1}^{n} b_i\right)^{-1} \left((M(x))\right) \left(\sum_{i=1}^{n} q_i x_i + \right. \\ &\left. + \lambda\left(M^* - M(x)\right)\right), \end{aligned} \quad (3)$$

where λ is an arbitrary design parameter.

In order to state the corresponding theorem, we need to introduce the following concept of full outflow connectedness. A compartmental system (1) is said to be *fully outflow connected* if at every state x there is a path $i \to j \to k \to \cdots \to l$ with positive k_{ij}'s from every compartment i to some compartment l such that $q_l > 0$ (see (**?**)).

Theorem 1. (Bastin, 2002) Let (2) be a fully outflow connected compartmental system. Then, for the closed loop system (2)-(3) with arbitrary initial conditions $x(0) \in R_+^n$:

i) the iso-mass Ω_{M^*} is forward invariant;

ii) the state $x(t)$ is bounded for all $t > 0$ and converges to the iso-mass Ω_{M^*}.

In (Magalhaes, 2005), the control law (3) was applied for the target control of the neuromuscular blockade of patients undergoing surgery, by means of the infusion of *atracurium*.

However, even after a satisfactory identification of the patients characteristics, it was necessary to consider an additional integrator, in order to achieve good results. This might be explained by the fact that (contrary to what happens, for instance, with state feedback stabilisers, which are not uniquely defined from the system matrices) the control law (3) strongly depends on the system parameters. Since parameter uncertainty is present not only in this case, but in most of the applications, it is relevant to analyse the robustness of that control law.

3. MASS CONTROL UNDER UNCERTAINTY

In this section, we analyse the performance of the control law (3), proposed in (Bastin, 2002), in the presence of parameter uncertainties.

If we consider that we can precisely measure what is injected from the outside into the system, the parameters b_i are not subject to uncertainties. On the other hand, since the control law does not depend on the interactions between compartments, that is, it does not depend on the k_{ij}'s , we may assume that the only uncertain parameters are $q_1, \ldots, q_n$. Therefore, we shall assume that a control law (3) is designed for a nominal system

$$\dot{x} = (A + \Delta A)\, x + bu, \tag{4}$$

while the real system is given by

$$\dot{x} = Ax + bu, \tag{5}$$

being ΔA the matrix of parameter uncertainties. Note that, in this case, if $\Delta q_i = -\Delta A_{ii}, i = 1, ..., n$, the control law (3) becomes

$$\begin{aligned} u(x) &= \max\left(0, \tilde{u}(x)\right) \\ \tilde{u}(x) &= \left(\sum_{i=1}^{n} b_i\right)^{-1} \left(\sum_{i=1}^{n} (q_i + \Delta q_i)\, x_i + \right. \\ &\left. + \lambda\left(M^* - M(x)\right)\right). \end{aligned} \tag{6}$$

It turns out that, for suitable values of the design parameter λ, when the control law (6) is applied to (5), the asymptotical values of the system mass lay in an interval which is related to M^* as stated in the next theorem.

Theorem 2. (Sousa, 2007) Let (5) be a fully outflow connected compartmental system, $\Delta_{qmin} = \min\{\Delta q_i\}$, $\Delta_{qmax} = \max\{\Delta q_i\}$ and take the design parameter λ in (6) larger than Δ_{qmax}. Then, the state trajectories $x(t)$ of the closed loop system (5)-(6), with arbitrary initial conditions $x(0) \in R_+^n$, converge to the forward invariant set

$$\Omega = \left\{x \in R_+^n : M(x) \in I(M^*)\right\},$$

with $I(M^*) = \left[\frac{\lambda}{\lambda - \Delta_{qmin}} M^*, \frac{\lambda}{\lambda - \Delta_{qmax}} M^*\right]$.

The previous result, gives us sufficient conditions to generalize Theorem 1 for a wide class of uncertain compartmental systems of R^3. Indeed, if we consider fully outflow connected compartmental systems for which $q_i \neq 0, i = 1, 2, 3$ and $q_{min} + \Delta_{qmin} > \Delta_{qmax}$(which is a reasonable assumption for practical issues), it is possible to prove that, when the control law (6) is applied to (5), the system mass converges to a constant value in the aforementioned interval, which is related to M^* as stated in the next results.

Proposition 3. Consider that $q_{min} + \Delta_{qmin} > \Delta_{qmax}$. Take the design parameter λ in (6) larger than Δ_{qmax}. Then, when the control law (6) is applied to (5), there exists an instant $t_1 > 0$ such that, for $t \geq t_1$,

$$u(x(t)) = \tilde{u}(x(t)) \geq 0,$$

PROOF. According to 2, when the control law (6) is applied to (5), the asymptotical values of the system mass lay in the interval $I(M^*) = \left[\overline{M}_{min}, \overline{M}_{max}\right]$, providing the design parameter λ in (6) to be larger than Δ_{qmax}. This implies that, for every $\varepsilon > 0$, there exists an instant $t_1 > 0$ such that

$$M(x(t)) \in \left[\overline{M}_{min} - \varepsilon, \overline{M}_{max} + \varepsilon\right],$$

for $t \geq t_1$.

Note that

$$\begin{aligned} &\tilde{u}(x) \geq 0 \Leftrightarrow \\ &\Leftrightarrow \sum_{i=1}^{3} (q_i + \Delta q_i)\, x_i + \lambda\left(M^* - M(x)\right) \geq 0 \\ &\Leftrightarrow \sum_{i=1}^{n} (\lambda - q_i - \Delta q_i)\, x_i \leq \lambda M^*. \end{aligned}$$

Since, for $t \geq t_1$,

$$\begin{aligned} &\sum_{i=1}^{n} (\lambda - q_i - \Delta q_i)\, x_i(t) \leq \\ &\leq (\lambda - q_{min} - \Delta_{qmin})\left(\overline{M}_{max} + \varepsilon\right), \end{aligned}$$

and

$$\begin{aligned} &(\lambda - q_{min} - \Delta_{qmin})\left(\overline{M}_{max} + \varepsilon\right) \leq \lambda M^* \Leftrightarrow \\ &\Leftrightarrow \varepsilon \leq \frac{\lambda}{\lambda - q_{min} - \Delta_{qmin}} M^* - \overline{M}_{max} \\ &\Leftrightarrow \varepsilon \leq \frac{\lambda}{\lambda - q_{min} - \Delta_{qmin}} M^* - \frac{\lambda}{\lambda - \Delta_{qmax}} M^*, \end{aligned}$$

if we take $\varepsilon_1 = \frac{\lambda}{\lambda - q_{min} - \Delta_{qmin}} M^* - \frac{\lambda}{\lambda - \Delta_{qmax}} M^*$ it follows that, if $\varepsilon \leq \varepsilon_1$, $\tilde{u}(x(t)) \geq 0$. Thus, considering $t_1 > 0$ such that, for $t \geq t_1$,

$$M(x(t)) \in \left[\overline{M}_{min} - \varepsilon_1, \overline{M}_{max} + \varepsilon_1\right],$$

we guarantee that, for $t \geq t_1$, $u(x) = \tilde{u}(x) \geq 0$. Note that, as $q_{min} + \Delta_{qmin} > \Delta_{qmax}$, $\varepsilon_1 > 0$. $\square$

In the following, we will only consider compartmental systems of R^3.

Take $k = \left(\sum_{i=1}^{3} b_i\right)^{-1}$ and consider the following points:

$$\bar{x_1} = \left[\alpha_1 \bar{x_{13}} \quad \alpha_2 \bar{x_{13}} \quad \bar{x_{13}}\right]^T,$$

with

$$\alpha_1 = \frac{k_{21} + b_1 k q_2}{q_1 + k_{12} + k_{13} - b_1 k q_1}\alpha_2 + \\ + \frac{k_{31} + b_1 k q_3}{q_1 + k_{12} + k_{13} - b_1 k q_1}$$

$$\alpha_2 = \frac{b_2 k \left(q_1 q_3 + q_3 k_{13} + q_1 k_{31}\right)}{\alpha_3} + \\ + \frac{\left(b_2 k + b_1 k\right) q_3 k_{12}}{\alpha_3} + \\ + \frac{k_{32}\left[q_1\left(1 - b_1 k\right) + k_{12} + k_{13}\right] + k_{12} k_{31}}{\alpha_3}$$

$$\alpha_3 = \left(1 - b_1 k - b_2 k\right)\left(q_2 q_1 + q_2 k_{12} + k_{21} q_1\right) + \\ + q_2 k_{13} + k_{21} k_{13} + k_{23}\left[q_1\left(1 - b_1 k\right) + k_{12} + k_{13}\right]$$

$$\bar{x_{13}} = \frac{\lambda M^*}{\left(\lambda - \Delta q_1\right)\alpha_1 + \left(\lambda - \Delta q_2\right)\alpha_2 + \left(\lambda - \Delta q_3\right)}.$$

$$\bar{x_2} = \left[\alpha_1 \bar{x_{22}} \quad \bar{x_{22}} \quad 0\right]^T,$$

with

$$\alpha_1 = \frac{k_{21} + b_1 k q_2}{q_1 + k_{12} - b_1 k q_1}$$
$$\bar{x_{22}} = \frac{\lambda M^*}{\left(\lambda - \Delta q_1\right)\alpha_1 + \left(\lambda - \Delta q_2\right)}$$

and

$$\bar{x_3} = \left[\frac{\lambda M^*}{\lambda - \Delta q_1} \quad 0 \quad 0\right]^T.$$

Proposition 4. If $q_i \neq 0, i = 1, 2, 3$, $q_{min} + \Delta_{qmin} > \Delta_{qmax}$ and if the design parameter λ in (6) is larger than $\Delta_{qmax} = \max\{\Delta q_i\}$, the closed loop system (5)-(6) has a unique equilibrium point that belongs to the set $\left\{x \in R_+^3 : \frac{dM(x)}{dt} = 0\right\}$. If the third component of $b = [b_1\ b_2\ b_3]^T$ is positive or if it is zero but there is something coming into that compartment, then, the equilibrium point is of the form $\bar{x_1}$. If the third component of $b = [b_1\ b_2\ b_3]^T$ is zero and $k_{13} = k_{23} = 0$, that is, if there is nothing coming into that compartment, then, there are two cases to be considered:

- the equilibrium point is of the form $\bar{x_2}$ if the second component of b is positive or if it is zero but there is something coming into that compartment, that is, $k_{12} \neq 0$
- the equilibrium point is of the form $\bar{x_3}$ if the second component of b is zero and there is nothing coming into that compartment, that is, $k_{12} = 0$.

□

PROOF. According to Proposition 3, there exists an instant $t_1 > 0$ such that, for $t \geq t_1$, $u(x(t)) = \tilde{u}(x(t)) \geq 0$. Thus, for $t \geq t_1$,

$$\frac{dM(x(t))}{dt} = 0 \Leftrightarrow \\ \Leftrightarrow \sum_{i=1}^{3} \Delta q_i x_i(t) + \lambda\left(M^* - M(x(t))\right) = 0 \\ \Leftrightarrow \left(\lambda - \Delta q_1\right) x_1(t) + \left(\lambda - \Delta q_2\right) x_2(t) + \\ + \left(\lambda - \Delta q_3\right) x_3(t) = \lambda M^*$$

and the equilibrium points of (5)-(6) that belong to the set $\left\{x \in R_+^3 : \frac{dM(x)}{dt} = 0\right\}$ are the solutions of the system

$$\begin{cases} Ax + bu = 0 \\ \dfrac{dM(x)}{dt} = 0 \end{cases}. \tag{7}$$

But, in this case,

$$u(x) = \tilde{u}(x) = \\ = \left(\sum_{i=1}^{3} b_i\right)^{-1}\left(\sum_{i=1}^{3}\left(q_i + \Delta q_i\right) x_i + \lambda\left(M^* - \right.\right. \\ \left.\left. - M(x)\right)\right) \\ = \left(\sum_{i=1}^{3} b_i\right)^{-1}\left(\sum_{i=1}^{3} q_i x_i\right) \\ = \left(\sum_{i=1}^{3} b_i\right)^{-1}\left[q_1\ q_2\ q_3\right] x,$$

thus, (7) becomes

$$\begin{cases} \left(A + b\left(\sum_{i=1}^{3} b_i\right)^{-1}\left[q_1\ q_2\ q_3\right]\right) x = 0 \\ \left(\lambda - \Delta q_1\right) x_1(t) + \left(\lambda - \Delta q_2\right) x_2(t) + \\ \quad + \left(\lambda - \Delta q_3\right) x_3(t) = \lambda M^* \end{cases}.$$

and it is easy to verify that, for each mentioned case, $\overline{x_1}$, $\overline{x_2}$ and $\overline{x_3}$ are the only solutions of this system. □

Theorem 5. Consider that $q_i \neq 0, i = 1, 2, 3$ and $q_{min} + \Delta_{qmin} > \Delta_{qmax}$. For each situation mentioned in Proposition 4, the state trajectories $x(t)$ of the closed loop system (5)-(6), with arbitrary initial conditions $x(0) \in R_+^3$, converge to the corresponding equilibrium point $\overline{x_1}$, $\overline{x_2}$, or $\overline{x_3}$, providing the design parameter λ in (6) to be larger than $\Delta_{qmax} = \max\{\Delta q_i\}$.

Corollary 6. Consider that $q_i \neq 0, i = 1, 2, 3$ and $q_{min} + \Delta_{qmin} > \Delta_{qmax}$ and let $\overline{M_1}$, $\overline{M_2}$ and $\overline{M_3}$ be the total mass of the system in $\bar{x_1}$, $\bar{x_2}$ and $\bar{x_3}$, respectively.
Then, the state trajectories $x(t)$ of the closed loop system (5)-(6), with arbitrary initial conditions $x(0) \in R_+^n$, converge to $\left\{x \in R_+^3 : M(x) = \overline{M_1}\right\}$, $\left\{x \in R_+^3 : M(x) = \overline{M_2}\right\}$ or to $\left\{x \in R_+^3 : M(x) = \overline{M_3}\right\}$, providing the design parameter λ in (6) to be larger than $\Delta_{qmax} = \max\{\Delta q_i\}$.

PROOF. It is only necessary to note that $\overline{M_1}$ is the total mass of the system in $\bar{x_1}$, $\overline{M_2}$ is the total mass of the system in $\bar{x_2}$ and $\overline{M_3}$ is the total system mass of the system in $\bar{x_3}$. The convergence to the aforementioned iso-masses follows from Theorem 5. □

In the following, we prove Theorem 5.

PROOF. Suppose that the third component of $b = [b_1\ b_2\ b_3]^T$ is positive or that it is zero but there is something coming into that compartment. Let $\bar{x_1}$ be the equilibrium point mentioned in (4),

$$\overline{M_1} = \frac{(\alpha_1 + \alpha_2 + 1)\,\lambda M^*}{(\lambda - \Delta q_1)\,\alpha_1 + (\lambda - \Delta q_2)\,\alpha_2 + (\lambda - \Delta q_3)}$$ be

the total mass of the system in $\bar{x_1}$ and take $k = \left(\sum_{i=1}^{3} b_i\right)^{-1}$.

Take t_1 such that, for $t \geq t_1$, $u(x(t)) = \tilde{u}(x(t)) \geq 0$ (the existence of such an instant is guaranteed by (3)). Since

$$\begin{aligned}
&M^* = \\
&= \frac{(\lambda - \Delta q_1)\,\alpha_1 + (\lambda - \Delta q_2)\,\alpha_2 + (\lambda - \Delta q_3)}{(\alpha_1 + \alpha_2 + 1)\,\lambda}\overline{M_1} \\
&= \overline{M_1} - \frac{\Delta q_1 \alpha_1 + \Delta q_2 \alpha_2 + \Delta q_3}{(\alpha_1 + \alpha_2 + 1)\,\lambda}\overline{M_1},
\end{aligned}$$

for $t \geq t_1$

$$\begin{aligned}
&u(x(t)) = \tilde{u}(x(t)) = \\
&= k\left[\sum_{i=1}^{3} (q_i + \Delta q_i)\, x_i(t) + \lambda\,(M^* - M(x(t)))\right] \\
&= k\left[\sum_{i=1}^{3} q_i x_i(t) + \sum_{i=1}^{n} \Delta q_i\,(x_i(t) - \bar{x_{1i}}) + \right.\\
&\quad \left. + \lambda\left(\overline{M_1} - M(x(t))\right)\right] \\
&= k\,[[q_1\, q_2\, q_3]\, x(t) + [\Delta q_1\, \Delta q_2\, \Delta q_3]\,(x(t) - \bar{x_1}) + \\
&\quad + \lambda\,[1\,1\,1]\,(\bar{x_1} - x(t))]
\end{aligned}$$

and

$$\begin{aligned}
&\overbrace{(x(t) - \bar{x_1})}^{\cdot} = \\
&= Ax(t) + bu - (A + bk\,[q_1\, q_2\, q_3])\,\bar{x_1} \\
&= Ax(t) + b\,[k\,[q_1\, q_2\, q_3]\, x(t) + \\
&\quad + k\,[\Delta q_1\, \Delta q_2\, \Delta q_3]\,(x(t) - \bar{x_1}) + \\
&\quad + k\lambda\,[1\,1\,1]\,(\bar{x_1} - x(t))] \\
&\quad - (A + bk\,[q_1\, q_2\, q_3])\,\bar{x_1} \\
&= (A + bk\,[q_1\, q_2\, q_3] + bk\,[\Delta q_1\, \Delta q_2\, \Delta q_3] - \\
&\quad - bk\lambda\,[1\,1\,1])\,(x(t) - \bar{x_1}) \\
&= \bar{A}\,(x - \bar{x_1})\,(t).
\end{aligned}$$

Since it can be easily seen that, for $\lambda > \Delta_{qmax}$, all the eigenvalues of $\bar{A}$ lie in C^-, it turns out that $\bar{A}$ is asymptotically stable and hence $(x - \bar{x_1})\,(t) \rightarrow 0$or, equivalently, $x(t) \rightarrow \bar{x_1}$.

To prove the convergence to $\bar{x_2}$ or to $\bar{x_3}$, we only need to consider the total mass of the system in $\bar{x_2}$ and in $\bar{x_3}$, that is,

$$\overline{M_2} = \frac{(\alpha_1 + 1)\,\lambda M^*}{(\lambda - \Delta q_1)\,\alpha_1 + (\lambda - \Delta q_2)}$$

and

$$\overline{M_3} = \frac{\lambda M^*}{\lambda - \Delta q_1}$$

and the proof will follow as in the previous case.

□

Note that, in this case, we may bound the absolute mass offset by $\frac{|\Delta_{qmax}| M^*}{\lambda - \Delta_{qmin}}$ and, clearly, it tends to zero when the uncertainties go to zero; moreover, increasing the design parameter λ contributes to increase the robustness of the control law.

3.1 *Case Study - mass control in neuromuscular relaxant administration*

In this section, some simulation examples are presented for the control of the administration of the neuromuscular relaxant drug *atracurium* to patients undergoing surgery. It is possible to model this problem as a three compartmental model that can be described as depicted in Fig. 2, where u is the drug infusion dose administered in the central compartment, and $k_{12}, k_{21}, k_{13}, q_3$ are positive micro-rate constants and q_1, q_2 are nonnegative micro-rate constants that vary from patient to patient.

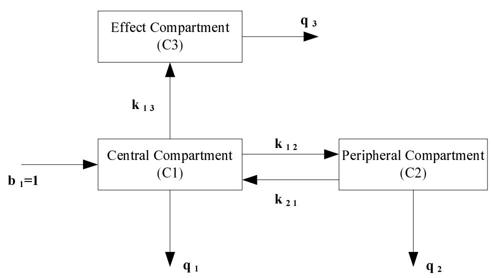


Fig. 2. Compartmental model for the neuromuscular blockade effect of the drug *atracurium*.

We consider the following values for the parameters (units $= min^{-1}$): $k_{12} = 0.1928, k_{13} = 0.0017, k_{21} = 0.1556, q_1 = 0.1047, q_2 = 0.1, q_3 = 0.0836$.

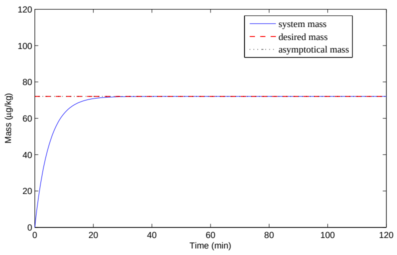
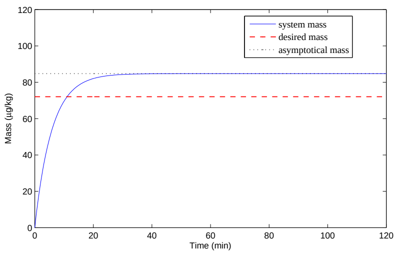


Fig. 3. Simulation for the neuromuscular blockade control, considering $\Delta q_i = 0, i = 1, 2, 3$.

(a)



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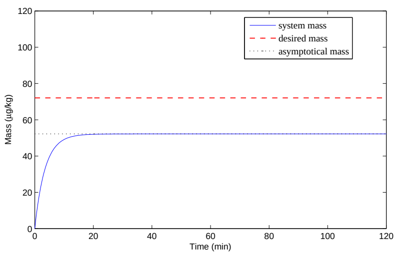

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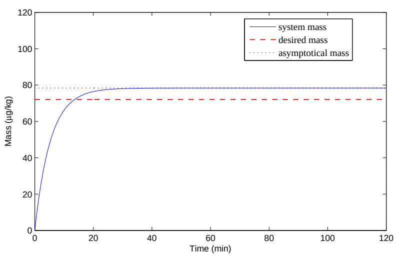


Fig. 4. Simulations for the neuromuscular blockade control. (a) Simulation with $\Delta q_i = 0.03, i = 1, 2, 3.$; the system mass reaches the set-point $\overline{M_1} = 84.7662$. (b) Simulation with $\Delta q_1 = -0.09, \Delta q_2 = -0.03$ and $\Delta q_3 = -0.02$; the system mass reaches the set-point $\overline{M_1} = 52.2288$. (c) Simulation with $\Delta q_1 = 0.02, \Delta q_2 = 0$ and $\Delta q_3 = 0.05$; the system mass reaches the set-point $\overline{M_1} = 78.3715$.

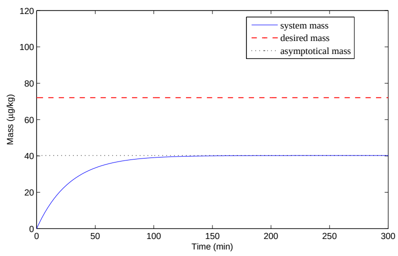
Our aim is to stabilise the system mass on the value $M^* = 72.0513$ (which, in an exact modelling situation, would correspond to the typical 10% level of neuromuscular blockade), using the control law (6). We start by taking the design parameter $\lambda = 0.2$.

In the first simulation, depicted in Fig. 3, it is assumed that the nominal patient model coincides with the real one, i.e., $\Delta q_i = 0, i = 1, 2, 3$. As expected, the system mass converges to M^*.

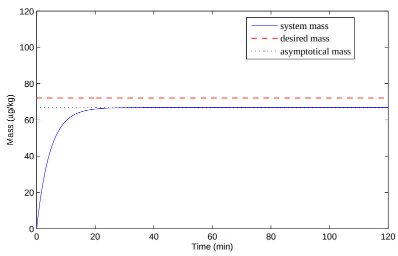
The first simulation in Fig. 4 corresponds to the case where the Δq_i's are taken to be all equal, namely $\Delta q_1 = \Delta q_2 = \Delta q_3 = 0.03$. The second and the third simulations in Fig. 4 correspond to the case where the Δq_i's are different.

Finally, Fig. 5 illustrates the behavior of the mass of the controlled system for different values of the parameter λ, under a fixed uncertainty for the system parameters. According to the definition of $\overline{M_1}$, one observes that the increasing of λ corresponds to the decrease of the final mass offset.

(a)



(b)



(c)

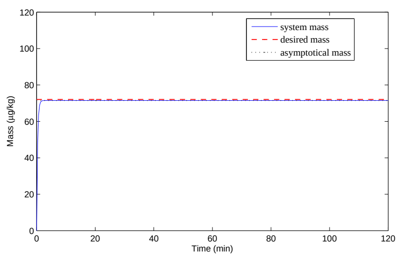


Fig. 5. Simulations for the neuromuscular blockade control. These simulations where obtained considering $\Delta q_1 = -0.02, \Delta q_2 = 0$ and $\Delta q_3 = -0.03$, and different values of λ. (a) Simulation for $\lambda = 0.02$. (b) Simulation for $\lambda = 0.2$. (c) Simulation for $\lambda = 2$.

4. CONCLUSION

This paper presents a study of the performance of the control law (3) proposed in (Bastin, 2002) when applied to the mass control of compartmental systems with parameters uncertainties.

It turns out that the asymptotical mass values converge to a positive constant value that can be expressed in terms of the parameter uncertainties and of the desired mass. This allows to derive bounds for the asymptotical mass offset that can be made arbitrarily small, provided that the uncertainties in the parameter values are sufficiently small.

In order to illustrate the obtained results, simulations for the control of the administration of the neuromuscular relaxant drug *atracurium* to patients undergoing surgery were carried out.

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